BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problems Mailbox.

Translated from Japanese by the Ralph McElroy Co., Custom Division
P.O. Box 4828, Austin, Texas 78765 USA

Code: 282-59319

JAPANESE PATENT OFFICE
PATENT JOURNAL
KOKAI PATENT NO. HEI 4[1992]-182423

Int. Cl.[5]:	A 61 K 7/50 31/16 31/195 //A 61 K 35/78 C 11 D 3/48
Sequence Nos. for Office Use:	7252-4C 8413-4C 8413-4C 7180-4C 7614-4H
Application No.:	Hei 2[1990]-311040
Application Date:	November 16, 1990
Publication Date:	June 30, 1992
No. of Claims:	1 (Total of 7 pages)
Examination Request:	Not requested

COMPOSITION FOR CLEANING AND WIPING

Inventors:

Eriko Kasahara
Shiseido Co., Ltd.
Research Center,
1050 Shinbane-cho,
Kohoku-ku, Yokohama-shi,
Kanagawa-ken

Kenji Kitamura
Shiseido Co., Ltd.
Research Center,
1050 Shinbane-cho,
Kohoku-ku, Yokohama-shi,
Kanagawa-ken

Yasukazu Nakayama
Shiseido Co., Ltd.
Research Center,
1050 Shinbane-cho,
Kohoku-ku, Yokohama-shi,
Kanagawa-ken

Naoe Akiyama
Shiseido Co., Ltd.
Research Center,
1050 Shinbane-cho,
Kohoku-ku, Yokohama-shi,
Kanagawa-ken

Applicant:

Shiseido Co., Ltd.
7-5-5 Ginza, Chuo-ku,
Tokyo

[There are no amendments to this patent.]

Claim

1. Composition for cleaning and wiping characterized by containing one or more compounds having protease inhibitory action.

Detailed explanation of the invention

Industrial application field

This invention pertains to a novel composition for cleaning and wiping. In particular, it pertains to a composition for cleaning and wiping having excellent effectiveness and safety, which comprises one or more compounds having a protease inhibitory action as an effective component, is effective for removing any residual excreta remaining at the periphery of the anus, etc., after wiping excreta with conventional toilet paper, etc., at the time of urination or defecation and thus preventing various symptoms such as inflammation, itching, etc.

Prior art

Previously, toilet paper has been generally used for removal of excreta after urination or defecation, and warm-water cleaners as well as cleaning cottons are also partially used. However, such warm-water cleaners are expensive, the usage is somewhat troublesome, and consequently, not popular. Furthermore, if toilet paper alone is used, it is not only impossible to remove excreta completely but also it is easy to generate delicate frictional scratches on the skin which cause itching,

inflammation, abrasion, etc., at the periphery of the anus and thus, it is not desirable.

Furthermore, in the case of infants and elderly persons with diapers, paper material such as toilet paper and cleaning cottons are generally used to wipe excreta. The excreta comes into contact with the skin for a relatively long period of time in the case of infants and elderly persons with diapers, thus, the excreta itself causes irritation, and the anus and its periphery frequently have symptoms of inflammation, abrasion, itching, etc.

As a means to solve this problem, there are known cleaners in the form of aerosols, wet tissue paper, oil, etc., and they have good cleaning effects but some cause irritation or inflammation becoming undesirable with respect to safety.

Problems to be solved by the invention

The inventors of this invention studied diligently under the circumstances described above, and as a result, they found it possible to prepare a composition having excellent cleaning power and remarkaly reduced skin irritation by compounding those cleaners in the form of aerosols, wet tissue, oil, etc., with compounds having a protease inhibitory action, and they arrived at this invention.

Means to solve the problems

Specifically, this invention is a composition for cleaning and wiping characterized by containing one or more compounds having protease inhibitory action.

The configuration of this invention is explained as follows.

The cleaning and wiping composition of this invention is a composition especially suitable for disinfection and cleaning of skin portions such as the anus and periphery, genitalia and periphery, underarm, etc., where it is generally not easy to clean and wipe, and preventing inflammation, itching, etc., by cleaning these skin portions and keeping them clean.

Protease or protein decomposition enzyme is a generic name for those enzymes catalyzing hydrolysis of peptide bonds. Proteases can be subclassified into peptidases and proteinases. The former is an enzyme catalyzing cleavage of peptide bonds from the outside of the amino or carboxyl end of a protein or peptide, and the latter is an enzyme enabling cleavage of specific bonds inside a peptide chain. Furthermore, this proteinase is customly called a broadly defined name of "protease" in many cases, and depending on the its active site property, it is possible to subclassify into 4 kinds, that is, (1) serine type, (2) thiol (cysteine) type, (3) carboxyl type and (4) metal type proteinases, and there are respective specific inhibitors.

The protease inhibitors of this invention are all chemical substances which can inhibit reversibly or irreversibly the hydrolytic action of the above protease or protein decomposition enzyme.

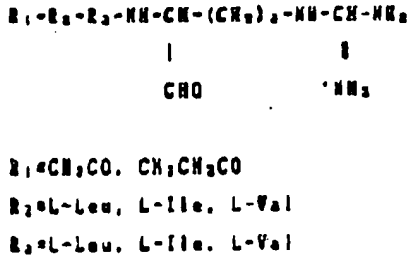
Specifically, there are the following substances:

(1) Compounds of animal or plant origin

There are preferably bovine pancreatin basic trypsin inhibitor, aprotinin, soybean trypsin inhibitor, lima bean protease inhibitor, corn protease inhibitor, etc.

(2) Compounds of microorganism origin

There are preferably antipain, plasminostreptin, compounds generically called leupeptin represented by the following general formula, etc.



(Leu: leucine, Ile: isoleucine, Val: valine)

(3) Benzamidine and its derivatives

There are preferably benzamidine, p-aminobenzamidine, m-aminobenzamidine, phenylguanidine, (2R,4R)-4-methyl-1-[N^2-(3-methyl-1,2-3,4-tetrahydro-8-quinolinesulfonyl)-L-alginyl]-2-piperidinecarboxylic acid monohydrate, dansylarginine N-(3-ethyl-1,5-pentanyl)amide, etc.

(4) Acetamide and its derivatives

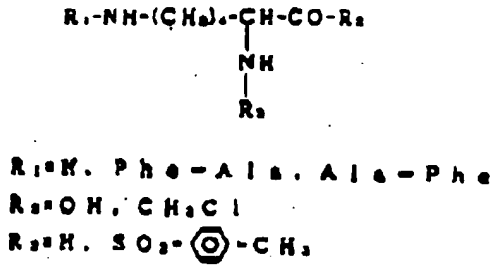
There are preferably acetamide, 2-phenylacetamide, cyclohexylchioxamide [transliteration], etc.

(9) Guanidinobenzoic acid and its derivatives

There are preferably p-nitrophenyl-p'-guanidinobenzoic acid, 3',6'-bis[4-guanidinobenzoyloxy)-5-(N'-4-carboxyphenyl)-thioureidospiro[isobenzofuran-1(3H),9'-(9H) xanthane]-3-one, etc.

(10) Lysine and its derivatives

There are preferably compounds represented by the following general formula:

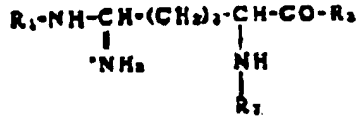


(Phe: phenylalanine, Ala: alanine)

It is not necessarily limited to these compounds in this invention, and among lysine and its derivatives, the effects of the compound with R_2 = CH_2Cl are especially excellent.

(11) Arginine and its derivatives

There are preferably compounds represented by the following general formula:



R_1 = H, D-Phe-Pro, Glu-Gly, Ile-Glu-Gly, Pro-Phe, Ala-Phe

R_2 = OH, CH_2Cl

R_3 = H, SO_2-  -CH_3

(Phe: phenylalanine, Pro: proline, Glu: glutamic acid, Gly: glycine, Ile: isoleucine, Ala: alanine)

It is not necessarily limited to these compounds in this invention, and among arginine and its derivatives, the effects of the compound with R_2 = CH_2Cl are especially excellent.

In this invention, these proteinase inhibitors may be used alone or as a mixture of two or more kinds.

The amount of such protease inhibitors to be compounded in the cleaning and wiping composition of this invention is desirably 0.0001-20 wt%, preferably 0.001-5 wt% of the whole amount of the composition. If it is less than 0.0001 wt%, the effects of this invention are not sufficient, and if it is over 20 wt%, it is undesirable with respect to formulation process, and it is disadvantageous with respect to cost.

The composition for cleaning and wiping agent of this invention may be compounded, in addition to protease inhibitors, with pharmaceutically allowable surfactants (anionic, cationic, nonionic, ampholytic and semipolar), antiseptics and antifungicides, sequestering agents, antistatic agents, antisedimentation agents, antioxidants, perfumes, moisture-retention agents, anti-inflammatory agents, sterilizers, vitamins and other drugs, if necessary, within the range causing no adverse effects on the effects of this invention.

Specific examples of such additives are as follows. For example, as anionic surfactants, there are the following compounds.

i) Fatty acid soap-type anionic surfactants represented by the following general formula:

RCOOM

(In the formula, R is an alkyl or alkenyl group having 8-18 carbon atoms, M is an alkali metal, organic amine or basic amino acid alone or a mixture of two or more kinds.)

ii) Ether carboxylate-type anionic surfactants represented by the following general formula

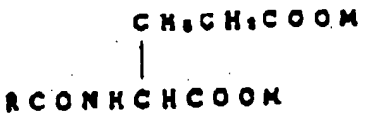
$$R(OCH_2CH_2)_nOCH_2COOM$$

(In the formula, R is an alkyl or alkylaryl group having 8-22 carbon atoms, n is 0 or an integer of 1-16, M is an alkali metal, organic amine or basic amino acid alone or a mixture of two or more kinds.)

iii) N-Acylsarcosinate-type anionic surfactants represented by the following general formula:

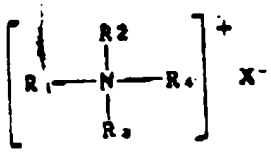
(In the formula, R is an alkyl or alkenyl group having 8-18 carbon atoms, M is an alkali metal, organic amine or basic amino acid alone or a mixture of two or more kinds.)

iv) Anionic surfactants having a $-COO^-$ group such as condensation products of higher fatty acids such as N-acylglutamate represented by the following general formula with amino acids:



(In the formula, R is an alkyl or alkenyl group having 8-18 carbon atoms, M is an alkali metal, organic amine or basic amino acid alone or a mixture of two or more kinds.)

As cationic surfactants, there are monoalkyl quaternary ammonium salts represented by the following general formula:



(where R_1 is an alkyl or alkenyl group having 12-22 carbon atoms, R_2, R_3 and R_4 are methyl or ethyl groups, X is a halogen atom or methylsulfate residual group), fatty acid amine salts, aromatic quaternary ammonium salts, pyridinium salts, imidazolinium salts, etc.

As nonionic surfactants, there are glycerine fatty acid esters, sorbitan fatty acid esters, sorbitol fatty acid esters, sucrose fatty acid esters, polyoxyethylenes (abbreviated to POE, below) sorbitan fatty acid esters, polyoxyethylene glycol fatty acid esters, POE alkyl ethers, POE alkyl phenyl ethers, POE-hardened castor oil derivatives, mannitol hydroxyfatty acid ethers, alkyl glucoside fatty acid ethers, etc.

As ampholytic surfactants, there are carboxybetaines such as N,N-dimethyllauryl-N-carboxymethylammonium betaine, N,N-dimethyl-N-oleyl-N-carboxymethylammonium betaine, lauryldimethylaminoacetic acid, etc.; imidazoline derivatives such as 2-lauryl-N-carboxyethyl-N-hydroxyethylimidazolium betaine, 2-lauryl-N-carboxymethyl-N-hydroxyethylimidazolium betaine, sodium 2-undecyl-N,N,N-(hydroxyethylcarboxymethyl)-2-imidazoline, 2-cocoyl-2-imidazoliumhydroxide-1-carboxyethyloxy-2-sodium, etc.; aminocarboxylates such as sodium N-coconut alkyl-β-aminopropionate, sodium N-coconut alkyl-β-iminodipropionate, etc.; sulfobetaine; aminobetaine; etc.

As semipolar surfactants, there are lauryldimethylamine oxide, stearyldimethylamine oxide, bis-(2-hydroxyethyl)laurylamine oxide, etc.

As a propellant, any propellant used for conventional aerosol products is usable. Specifically, there are fluorocarbons such as Flon 11 (registered trademark), Flon 12 (registered trademark), Flon 21 (registered trademark), Flon 113 (registered

trademark), Flon 114 (registered trademark), liquefied petroleum gas (LPG) which is a mixture of propane, isobutane and normal butane, dimethyl ether, compressed carbon dioxide, nitrogen, etc. These compounds may be used alone or as a suitable mixture of 2 or more kinds. The amount compounded is generally 2-20 wt%. If it is below 2%, the inner pressure is too low to provide good spraying until the stock solution is completely used. If it is over 20%, the effects are not especially improved further, and it is rather undesirable because of a high inner pressure.

As water-insoluble oily components, any conventionally used compounds are usable. Specifically, there are, for example, higher alcohols such as cetyl alcohol, stearyl alcohol, cholesterol, etc.; C_8-C_{22} higher fatty acids such as lauric acid, myristic acid, palmitic acid, stearic acid, oleic acid, isostearic acid, etc.; waxes such as solid paraffin, microcrystalline wax, polyethylene wax, candelilla wax, beeswax, hardened castor oil, carrauba wax, palico [transliteration] wax, etc.; animal or vegetable oils such as tallow, lard, leather oil, squalane, coconut oil, palm oil, palm core oil, soybean oil, olive oil, cotton seed oil, jojoba oil, castor oil, lanolin, etc.; mineral oils such as liquid paraffin, vaseline, etc.; and synthetic oils such as trimethylpropane triisostearate, isopropyl myristate, glycerol tri-2-ethylhexanate, pentaerythritol tetra-2-ethylhexanate, silicone oil, polyoxyethylene polyoxypropylene pentaerythritol ether, etc.

As polyhydric alcohols, any conventionally used alcohols may be used. For example, there are propylene glycol, dipropylene glycol, glycerol, 1,3-butylene glycol, polyethylene glycol, polyoxyethylene glycol, polyoxyethylene methylglycoside ether, polyoxyalkylene diglyceryl ether, polyoxyalkylene polyglyceryl

ether, polyoxyalkylene decaglyceryl ether, polyoxyalkylene pentaerythritol ether, sorbitol, maltitol, lactose, D-mannitol, etc.

In addition, sterilizers such as cetylpyridinium chloride, benzethonium chloride, dequalinium chloride, benzalkonium chloride, chlorhexidine gluconate, carbanilide, phenol, halogenated salicylanilide, etc.; moisturizers, for example, bases such as sodium hydroxide, ammonia, etc.; lower alcohols such as ethanol, etc.; mucopolysaccharides; pyrrolidone carboxylate, etc., are also usable.

The formulation of the cleaning and wiping composition of this invention may be any of those formulation suitable for accomplishing the objective as a cleaning and wiping agent, and for example, there are liquids (lotion, emulsion), creams, aerosols, wet tissues, sprays, etc.

Effect of the invention

The composition for cleaning and wiping of this invention has excellent effects preventing and improving rough skin; at the same time, it is highly safe and shows excellent cleaning and wiping power in the case of practical applications for cleaning and wiping.

Application examples

This invention is explained specifically in detail by using application examples as follows, but this invention is not necessarily limited to these examples.

Before explaining these application examples, those testing and evaluation methods carried out to evaluate the low irritation (prevention and improvement of rough skin formation) of the protease inhibitors of this invention are explained first as follows.

Practical use test

The test subjects were 60 infants of relatively tender skin liable to have "diaper rash" separated into 6 groups of 10 babies each. Diapers were used, and the genitalia, anus and their peripheries were cleaned with the cleaning and wiping compositions shown in Table I. Those application examples were used in 5 groups, and the Comparative Example 1 was used in the remaining one group. After carrying out a 4-week application test, the state and condition of the skin after 4 weeks were examined by naked eye examination, and the standards shown in Table II were used for evaluation. Incidentally, the formulation in each example was an aerosol formulation prepared using conventional procedures.

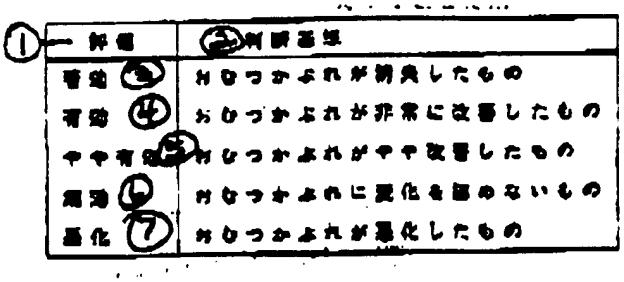
Table I

	1	2	3	4	5	6
1,3-ブチレングリコール	4.0	4.0	4.0	4.0	4.0	4.0
エタノール	20.0	20.0	20.0	20.0	20.0	20.0
ジメチルポリシロキサン	5.0	5.0	5.0	5.0	5.0	5.0
グリセリン	3.0	3.0	3.0	3.0	3.0	3.0
POEソルビタンモノステアリン酸エステル						
ソルビタン(EO:20mol)	2.0	2.0	2.0	2.0	2.0	2.0
メチルパラベン	0.1	0.1	0.1	0.1	0.1	0.1
香料	適量	適量	適量	適量	適量	適量
精製水	残余	残余	残余	残余	残余	残余
噴射剤 L.P.G.	7.0	7.0	7.0	7.0	7.0	7.0
ロイペプチン	0.05	—	—	—	—	—
トラネキサム酸	—	2.0	—	—	—	—
トシルリジルクロル メチルケトン	—	—	0.1	—	—	—
トシルアルギニン	—	—	—	3.0	—	—
ダイズトリプシン インヒビター	—	—	—	—	0.5	—

(The number in the table shows wt%)

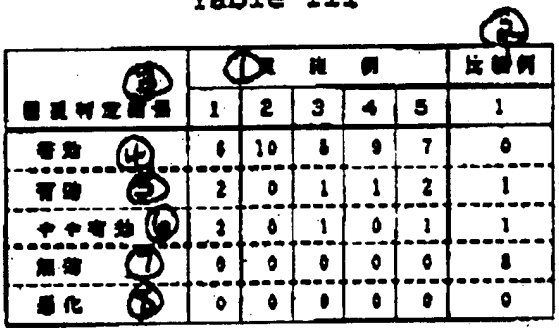
Key: 1 Application Example
2 Comparative Example
3 1,3-Butylene glycol
4 Ethanol
5 Dimethylpolysiloxane
6 Glycerol
7 POE sorbitan monostearate (EO: 20 mol)
8 Methylparaben
9 Perfume
10 Purified water
11 Propellant
12 Leupeptin
13 Tranexamic acid
14 Tosyl dichloromethyl ketone
15 Tosylarginine
16 Soybean trypsin inhibitor

Table II. Effects improving diaper rash



Key: 1 Evaluation
2 Evaluation standards
3 Markedly effective: diappearance of diaper rash
4 Effective: significantly improved diaper rash
5 Slightly effective: slightly improved diaper rash
6 Ineffective: no change in diaper rash
7 Worsening: worsening of diaper rash

Table III



	実施例 1	2	3	4	5	比較例 1
著効	6	10	8	9	7	0
有効	2	0	1	1	2	1
やや有効	2	0	1	0	1	1
無効	0	0	0	0	0	8
悪化	0	0	0	0	0	0

Key: 1 Application example
2 Comparative example
3 Naked eye examination result
4 Markedly effective
5 Effective
6 Slightly effective
7 Ineffective
8 Worsening

In the table, the number of subjects showing respective results of examination are represented.

As apparent from the results shown in Table III, the effectiveness of examples of the composition of this invention (Application Examples 1-5) was found to be apparently superior to that of the control composition (Comparative Example 1). Furthermore, the cleaning power of the composition of this invention was found to be excellent.

Application Example 6

Cleaning and wiping agent	wt%
(1) Purified water	remainder
(2) Glycerol	4.0
(3) Dipropylene glycol	7.0
(4) Ethanol	25.0
(5) Polyoxyalkylene-modified organopolysiloxane (polyoxyethylene group: 60 wt%, mean molecular weight of 10,000)	3.0
(6) Perfume	Suitable amount
(7) Tosyllysine	1.5

Application Example 7

Cleaning wet tissue stock solution

	wt%
(1) Purified water	remainder
(2) Ethanol	50.0
(3) p-Aminobenzamidine	0.08

(4) Perfume	Suitable amount

Application Example 8

Cleaning oil

	wt%
(1) Liquid paraffin	Remainder
(2) Neopentyl glycol dicaprate	8.0
(3) Squalane	2.5
(4) Olive oil	2.0
(5) Tocopherol acetate	0.1
(6) Cyclohexylguanidine	0.7

The safety and cleaning effects of Application Examples 6-8 were found to be excellent.